PB91-159681

Pesticide Fact Sheet Number 219: Tribenuron Methyl

(U.S.) Environmental Protection Agency, Washington, DC

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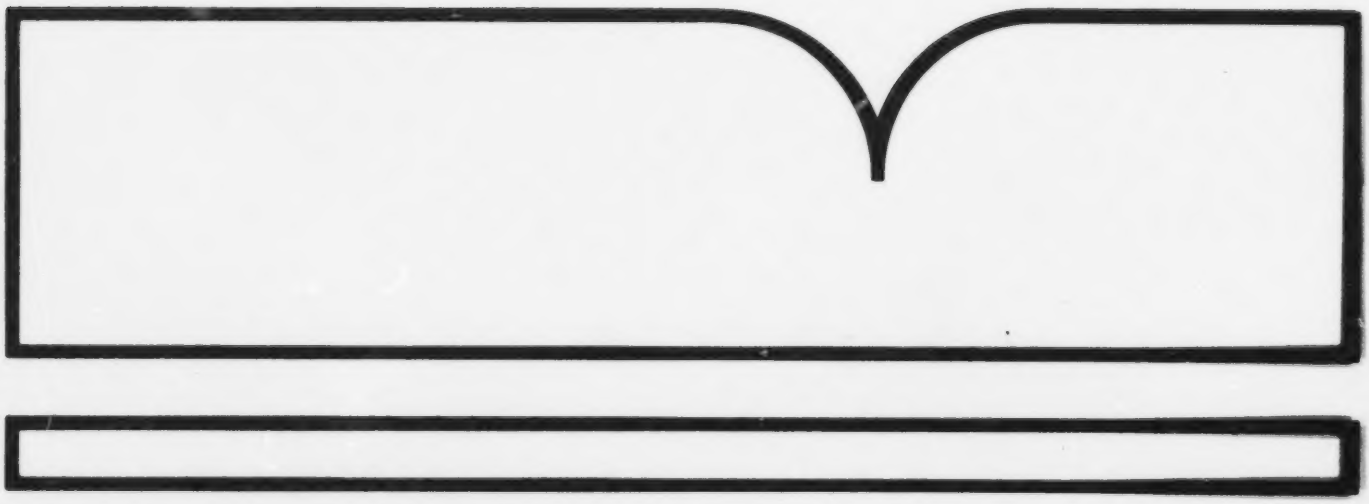

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16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

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EPA

Pesticide Fact Sheet

PB91-159681

Name of Chemical: Tribenuron Methyl
Reason for Issuance: New Chemical
Date Issued: June 30, 1989
Fact Sheet Number: 219

Description of Chemical

Chemical Name:	Methyl 2-[[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-methylaminolcarbonyl]amino] carbonyl]amino]sulfonyl]benzoate
Common and Other Names:	Tribenuron Methyl,L-5300
Trade Name:	Express
OPP (Shaughnessy) No.:	128887
Chemical Abstracts Service (CAS) Number:	101200-48-8
Molecular Weight:	395.40
Year of Initial Registration:	1989
Pesticide Type:	Herbicide
Chemical Family:	Sulfonylurea
U.S. and Foreign Producers:	E.I. du Pont de Nemours & Company,Inc.

Use Patterns and Formulations

Application Sites:	Terrestrial food crops
Major Crops Treated:	Wheat and barley
Type and Methods of Application:	Air or Ground
Application Rates:	0.125-0.250 or ai/acre (9-18 g ai/ha)
Types of Formulations:	75% Dry flowable powder
Usual Carriers:	Mix with Water

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U.S. DEPARTMENT OF COMMERCE
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Science Finding

Summary Science Statement

Express has low acute toxicity (Category IV) for acute dermal and acute oral toxicity. The product is a moderate eye irritant (Category III) and causes no skin irritation or skin sensitization. Express is a Group C carcinogen (possible human carcinogen) without quantification based on the incidence of mammary gland adenocarinomas in Sprague-Dawley strain rats. The Agency has determined that a quantitative carcinogenic risk assessment for this chemical is not appropriate because: a) the tumors were observed in one sex and one species; b) the tumors were significantly increased only at the highest dose tested at which the compound was clearly toxic and exceeded an adequately high dose for assessing carcinogenic potential; c) analog beside the s-triazine show little evidence of carcinogenic potential; d) quantification has not been found appropriate for the s-triazine analog; and e) there is a possible association between the induced tumors and hormonal effects at the highest test dose; and f) there was no evidence of genetic toxicity shown in several studies with the herbicide.

The Scientific Advisory Panel has placed "Express" in Group D because the only evidence for carcinogenicity was obtained with doses that greatly exceeded the maximum tolerated dose (MTD). The Panel noted that the negative data obtained with male rats and mice of both sexes and the lack of genetic toxicity also supported Category D. The Agency believes that the data on carcinogenicity for this chemical do not indicate a strong likelihood that this chemical poses a significant risk to human health. The chemical is not a developmental toxicant in rats or rabbits and is not considered mutagenic.

Express is practically nontoxic to birds, fish, aquatic invertebrates, and honey bees. The following studies are required because Express is to be applied by air for weed control in terrestrial food crops.

Plant Testing

Tier II	Seed Germination/Emergence	123-1
	Vegetative Vigor	123-1
	Aquatic Plant Growth	123-2

Fate Testing

Spray Drift - droplet size spectrum 201-1

Spray Drift - drift field evaluation 202-1

Express is not expected to reach ground water under normal use conditions,although the available data was considered insufficient to fully assess the leaching potential of EXPRESS. The following studies are required as part of the conditional registration.

Partially Satisfied

Aerobic Soil Metabolism - 162-1

Leaching and Adsorption/Desorption - 163-1

Partially Satisfied

Anaerobic Soil Metabolism - 162-2

Terrestrial Field Dissipation - 164-1

Not Satisfied

Anaerobic Soil Metabolism - 162-2

Terrestrial Field Dissipation - 164-1

The nature of the residue in plants and animals is adequately understood and adequate methodology is available for enforcement of the tolerance in/on barley grain, wheat grain, barley straw and wheat straw.

Chemical Characteristics of the Technical Material

	TECHNICAL (Tribenuron Methyl)
Molecular Weight:	395.40
Molecular Formula:	$C_{15}H_{17}N_5O_6S$
Color:	Off White
Physical State:	White crystalline Solid
Odor:	Slightly Pungent
Melting Point:	141° C
Density:	1.54 g/cc

Solubility: * solubility limits in organic solvents at 25•C

(acetone) 43.8 mg/L, (acetonitrile),54.2 mg/L g/, (Carbon Tetrachloride), 3.12 mg/L (Ethyl Acetate) 17.5 mg/L, (Hexane) 0.028 mg/L (Methanol), 3.39 mg/L

* solubility limits in water and aqueous buffer at 25•C * 28 mg/L (pH-4.0 buffer); *50 mg/L (pH-5.0 buffer); *280 mg/L (pH-6.0 buffer); *49 mg/L @ 20•C (pH-5.0 buffer); 2.04 g/L @ 20•C (pH-7.0 buffer); *18.3 g/L @ 20•C (pH-9.0 buffer).

Vapor Pressure: 4.0×10^{-10} millimeter Of Mercury

Dissociation Constant pKa: pKa value = 4.7

pH: 4.27 (slurry in water)

Stability: Relatively unstable in most solvents, especially aqueous solvents. Stable to metals. Relatively stable to sunlight

Octanol/Water Partition Coefficient: 0.30 @ pH - 7.0

Toxicology Characteristics

Acute Testing

Acute Oral Toxicity - Rat: > 5000 milligrams/kilogram/day (mg/kg/day) (males and females); Toxicity Category IV

Acute Dermal Toxicity - Rabbit: > 2000 mg/kg both sexes; Toxicity Category IV

Primary Dermal Irritation- Rabbit: Irritation cleared by 72 hours; Toxicity Category III

Primary Eye Irritation - Rabbit: Opacity and irritation cleared within 72 hours; Toxicity Category III

Dermal Sensitization - Guinea Pig: Nonsensitizing

Acute Inhalation: > 6.7 mg/L both sexes; Toxicity Category III

Acute Studies: Express Herbicide (75% DF Formulations):

Acute Oral Toxicity - Rat: 5700 mg/kg for males, 4800mg/kg for females; Toxicity Category IV males; III females

Acute Dermal Toxicity - Rabbit: > 2000 mg/kg both sexes; Toxicity Category III

Primary Eye Irritation - Moderately irritating; Toxicity Category III

Primary Dermal Irritation- Score 0; Toxicity Category IV

Acute Inhalation - Rat: Waived because of granule size

Dermal Sensitization - Guinea Pig: Not a sensitizer

Subchronic Toxicity
Data are available to satisfy the requirements for subchronic feeding studies. These data are discussed below.

Subchronic Toxicity
A 90-day rat subchronic feeding study conducted at dose levels of 0, 5, 87.5, and 250 mg/kg/day with a no-observable - effect level (NOEL) of 5 mg/kg/day and an lowest-observable effect level (LOEL) of 87.5 mg/kg/day.

A 90-day dog subchronic feeding study conducted at dose levels of 0, 1.25, 12.5, and 62.5 mg/kg/day with a NOEL of > 62.5 mg/kg/day (highest dose tested [HDT]).

Chronic Feeding and Oncogenicity Studies Data are available to satisfy the requirements for chronic feeding studies and oncogenicity studies in two species. These data are discussed below.

An 18-month oncogenity study in Charles River Crl:CD-1 (ICR)BR strain mice fed dosages of 0, 3,30, and 225 mg/kg/day with a NOEL of 3 mg/kg/day and an LOEL of 30 mg/kg/day based on decreased body weight gain in both sexes, an increased incidence of age-related effects (amyloidosis and thyroid inflammation in both sexes, testicular atrophy (seminiferous degeneration and oligospermia) and mortality in males given 225 mg/kg/day). No carcinogenic effects were observed in the study.

A 2-year feeding/oncogenic study in Sprague-Dawley rats fed dosages of 0, 1.25, 12.5, and 62.5 mg/kg/day with a statistically significant increase in the incidence of mammary gland adenocarcinomas in treated female rats at 62.5 mg/kg/day (HDT), a NOEL of 1.25 mg/kg/day and an LOEL of 12.5 mg/kg/day based on reduced body weight gains in treated males and females.

A 1-year feeding study in dogs fed dosage levels of 0, 0.625, 6.25, and 37.5 mg/kg/day with a NOEL of 0.625 mg/kg/day and a LOEL of 6.25 mg/kg/day (both sexes) based on elevated blood levels of bilirubin and aspartate aminotransferase (AST), increased urinary volume and decreased body weight gain in males, levels as well as decreased body weight gain.

Developmental toxicity and Reproduction: Data are available to satisfy the requirements for a two-generation reproduction study and teratology studies in two species. These studies are discussed below.

A teratology study in rats fed dosage levels of 0, 20, 125, and 500 mg/kg/day with a NOEL of 20 mg/kg/day (lowest dose tested [LDT]) for both maternal and developmental toxicity and an LOEL of 125 mg/kg/day. Maternal effects at the 125 and 500 mg/kg/day dose levels included decreased body weight gain and food consumption and an increased incidence of excess salivation; fetal effects include decreased body weights and increased numbers of resorptions (only at the HDT).

A teratology study in rabbits fed dosage levels of 0, 5, 20, and 80 mg/kg/day with a NOEL for maternal and developmental toxicity of 20 mg/kg/day, an LOEL for maternal and developmental toxicity of 80 mg/kg/day (HDT); maternal effects included decreased feed consumption and an increased incidence of abortions, and fetuses had slightly reduced body weights.

A two-generation reproduction study in rats with a NOEL of 1.25 mg/kg/day and a LOEL of 12.5 mg/kg/day based on decreased body weight gain; there were no reproductive or developmental effects observed at any dose level tested (HDT of 50 mg/kg/day).

Mutagenicity: Acceptable data are available for Express to satisfy the mutagenicity data requirements. These data are discussed below.

A gene mutation assay in Salmonella typhimurium and Chinese hamster ovary cells in vitro. These assays were negative; structural chromosomal damage, including a micronucleus test in mice and a cytogenetics assay in rats. Both assays were negative; an unscheduled DNA synthesis assay in rat primary hepatocytes in vitro. The assay was negative for genotoxicity.

Metabolism: A series of limited experiments suggested that Express is readily absorbed by male and female rats. The excretion half-Life at the low dose was 26 to 33 hours. Half-life values were similar in male and female rats and in rats given repeated daily doses (100 parts per million [ppm] for 21 days and 20 mg/kg on day 22). At high single doses (1700 to 2000 mg/kg) the excretion half-life for male rats was 51 to 54 hours, and for female rats 69 to 96 hours.

Tissue levels of Express and its metabolites increased with dose, but there was no concentration observed in any particular organ or tissue.

Major metabolites included metsulfuron methyl, saccharin, and O-dimethyl triazine amine. The major route of excretion in rats was the urine.

Physiological and Biochemical Characteristics:

Translocation and Absorption by Plants: Absorption through foliage. Metabolism/Persistence in Animals: Chemical and metabolites eliminated through the urine.

The Scientific Advisory Panel's Recommendation:

The Scientific Advisory Panel has recommended that "Express" be placed in Category D on the grounds that the only evidence for carcinogenicity was obtained with doses that greatly exceeded the MTD. The Panel noted that the negative data obtained with male rats and mice and the lack of positive genetic toxicity also supported Category D. The Agency believes that the data on carcinogenicity for this chemical do not indicate a strong likelihood that this chemical poses a significant risk to human health.

Agency's Classification For Oncogenicity:

Methyl 2-[[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2yl) methylamino] carbonyl]amino]sulfonyl]benzoate has been classified by the Agency into Group C (possible human Carcinogen) because of a statistically significant increase in the incidence of malignant tumors (mammary gland adenocarcinomas) in female Sprague-Dawley strain rats.

The increased incidence exceeded the historical control range. The Agency has determined that a quantitative carcinogenic risk assessment for this chemical is not appropriate because: 1) The tumors were observed only in one sex and one species; 2) the tumors were significantly increased only at the highest dose tested at which the compound was clearly toxic and exceeded a maximum adequately high dose to assess carcinogenic potential; 3) structural analog show little evidence of oncogenic potential; 4) quantification has not been found appropriate for the s-triazine analog; 5) there is a possible association between the induced tumors and a hormonal influence at the high test doses; and 6) in addition, there was no evidence of genetic toxicity shown in several studies.

Environmental Characteristics:

Hydrolysis: The solubility and stability of the active ingredient increases with increasing pH. The half-lives of degradation are less than 1 day at pH 5, 3-6 days at pH 7, and 32 days at pH 9. The hydrolytic mechanism involves cleavage of the sulfonylurea bridge to produce degradates that contain a single ring moiety: an ester sulfonamide (which contains the phenyl moiety) and triazine amine (which contains the triazine moiety). The ester sulfonamide can undergo further reactions depending on the pH (acid hydrolysis to form the acid sulfonamide and cyclization to form saccharin under basic conditions).

Photodegradation in Water and on soil

Photodegradation is not an important degradations mechanism for EXPRESS.

Microbial degradation:

Under both aerobic and anaerobic conditions, the degradation of EXPRESS in soils appears to be dominated by an abiotic (hydrolysis) process in which the pH of the soil controls the breakdown of the active ingredient. However, there is evidence indicating that the degradates are more prone to biodegradation than the parent and that the degradates containing the triazine moiety may be more persistent than those containing the phenyl moiety.

Mobility in soil:

Parent DPX-L5300 was mobil in columns of Fargo silty clay, Sassafras loamy sand, Gardena silty loam, and Chopart silt loam soils, with estimated kd values below 0.5 for all soils.

The degradate acid sulfonamide was also found to be mobile in these soils. Data is needed to assess the mobility of the triazine degradates.

Loss from volatilization:

Volatilization of parent pesticide from soils is expected to be minimal because of its low vapor pressure.

Field Dissipation Studies:

The available dissipation data was considered insufficient to fully assess the leaching potential of EXPRESS.
Data indicate that the active ingredient dissipated from the surface 0-5 inch soil depth with half-lives of 9 days in an alkaline (pH 8.3) Idaho silt loam soil and 5 days in a neutral (pH 7.3) Illinois silty clay loam soil. These studies were

considered supplemental and new studies have been required to fully assess the leaching potential of EXPRESS.

Bioaccumulation in fish:

Parent DPX-L5300 is not expected to bioaccumulate in fish because of the low octanol/water partition coefficient.

Accumulation in crops:

Parent DPX-L5300 was not detected in any plant tissue (small grains, leafy vegetables, root vegetable) at concentrations above the 10 ppb level-of-concern (detection limit $\leq$ 1 ppb) 18g

Ecological Characteristics:

Acceptable data are available to satisfy the requirements for an avian single dose acute oral toxicity study on one species; two subacute dietary toxicity studies on one species of waterfowl and one species of upland game bird; two 96-hour fish acute toxicity studies on two species of freshwater fish, preferably one coldwater species and one warmwater species; and a 8-hour acute toxicity study with freshwater invertebrates. Studies that satisfy these requirements are listed below.

Avian Acute Oral Toxicity: Bobwhite Quail LD_{50}>2250 mg/kg;

Avian Acute Dietary Toxicity: Mallard Duck LD_{50}> 5620 ppm and Bobwhite Quail > 5620 ppm;

Freshwater Fish Acute Toxicity: Bluegill Sunfish LC_{50}> 1000 ppm and Rainbow Trout LC_{50}> 1000 ppm; and Freshwater Invertebrate Toxicity: Daphnia magna LC_{50}720ppm.

Based on the above data, Express is practically nontoxic to birds on an acute and dietary basis, practically nontoxic to both warmwater and coldwater fish, and practically nontoxic to aquatic invertebrates.

The following studies are required because Express is to be applied by air for weed control in terrestrial food crops.

Plant Testing:

Tier II	Seed Germination/Emergence	123-1
	Vegetative Vigor	123-1
	Aquatic Plant Growth	123-2

Fate Testing:

Spray Drift - droplet size spectrum 201-1

Spray Drift - drift field evaluation 202-1

Tolerance Assessment: The nature of the residue in plants and animals has been adequately defined for the use on wheat and barley, and adequate analytical methods are available for enforcement purposes.

A tolerance is established for residue of the herbicide methyl 2-[[[[N-(methoxy-6-methyl-1,3,5-triazin-2-yl)methylamino] carbonyl]amino]sulfonyl]benzoate in or on the raw agricultural commodities wheat grain at 0.05 ppm, wheat straw at 0.10 ppm, barley grain at 0.05 ppm, and barley straw at 0.10 ppm.

The acceptable daily intake (ADI) was calculated to be 0.0063 mg/kg/day. This value was based on a NOEL of 0.625 mg/kg/day from the 1-year dog feeding study. An uncertainty factor of 100 was used to calculate the ADI.

The theoretical maximum residue contribution for this tolerance is calculated to be 0.000073 mg/kg/day. The current action will occupy 1.16 percent of the ADI. There are no published tolerances for this chemical. The pesticide is useful for the purposes of this tolerance rule.

Summary of Regulatory Position and Rationale:

The available data submitted to the Agency provide sufficient information to support conditional registration of the use on wheat and barley. Therefore, the Agency has accepted the use of Express on wheat grain, wheat straw, barley grain, and barley straw.

Conditions of registration are as follows: E.I. du Pont de Nemours & Company, Inc. will submit these additional studies and/or information with 27 months of the date of registration (June 30, 1989).

Aerobic Soil Metabolism - 162-1

Leaching and Adsorption/Desorption - 163-1

Anaerobic Soil Metabolism - 162-2

Terrestrial Field Dissipation - 164-1

Spray Drift-Droplet Size Spectrum - 201-1

Spray Drift-Drift Field Evaluation - 202-1

Tier II Seed Germination/Emergence - 123-1

Vegetative Vigor - 123-1

Aquatic Plant Growth - 123-2

Public Interest Statement:

Express is a low use rate sulfonylurea herbicide;

Express has an extremely wide postemergence application window to wheat and barley;

Express has broad-spectrum weed control activity;

Express has a short half-life;

Express is nonvolatile; and

Express is of low toxicity to man and animals.

B2/3

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DISCLAIMER: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy data requirements for pesticide registration and reregistration. The complete Registration Standard for the pesticide may be obtained from the contact person listed above.

END
DATE
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